

<b>Notice of References Cited</b>	Application/Control No. 09/820,954	Applicant(s)/Patent Under Reexamination	
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**U.S. PATENT DOCUMENTS**

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
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**NON-PATENT DOCUMENTS**

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X	U	The Merck Index, (10 <sup>th</sup> ed. 1983).
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# THE MERCK INDEX

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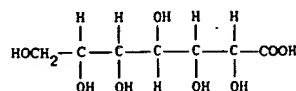
TENTH EDITION

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Ann. 270, 71 (1892); Armestar, C.A. 45, 2865 (1951). Process starting with calcium cyanide and glucose: Clevenot, U.S. pat. 2,735,866 (1956 to Lab. Clevenot).



Lactonizes upon evapn. The lactone forms large sweetish crystals, mp 145-148°.  $[\alpha]_D^{20} -56.0'$  (shows mutarotation). Sol in water.

Sodium salt,  $\text{C}_7\text{H}_{13}\text{NaO}_6$ , *glucoptate sodium*, *sodium glucoheptonate*. Prepn from corn sirup: Behnke, U.S. pat. 3,022,343 (1962 to Pfansthil Labs). Crystals ( $\alpha$ -form), dec 161°.  $[\alpha]_D^{20} +6.06'$  ( $c = 10$  in  $\text{H}_2\text{O}$ ). Freely sol in water.

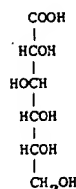
Calcium salt,  $\text{C}_{14}\text{H}_{26}\text{CaO}_{16}$ , *glucoptate calcium*, *calcium glucoheptonate*, *calcium glucosemonocarbonate*, *calcium glucomonocarbonate*, *Calheptose*. Prepn from Na salt: Holstein, U.S. pat. 3,033,900 (1962 to Pfansthil Labs.). Hygroscopic crystals, somewhat acid taste, dec 200°. Sol in water.

Magnesium salt,  $\text{C}_{14}\text{H}_{26}\text{MgO}_{16}$ , *magnesium glucoheptonate*, *magnesium glucosemonocarbonate*, *magnesium glucomonocarbonate*, *Navolin*. Prepn: Cipelli, U.S. pat. 3,063,896 (1962 to Merck & Co.). Water-sol crystals, pleasant taste.

Erythromycin salt, see Erythromycin Glucoheptonate.

THERAP CAT: Pharmaceutical aid.

**4316. Gluconic Acid.** D-Gluconic acid; dextronic acid; maltonic acid; glyconic acid; glycogenic acid; pentahydroxycaproic acid.  $\text{C}_6\text{H}_{12}\text{O}_7$ ; mol wt 196.16. C 36.74%, H 6.17%, O 57.10%. May be prepd from glucose by electrolytic oxidation in alkaline medium: Helwig, U.S. pat. 1,937,273 (1933); by chemical oxidation with hypobromites: Stoll, Kussmaul, U.S. pat. 1,648,368 (1927). At present produced in commercial quantities by the fermentative oxidation of the aldehyde group in glucose from corn using *Aspergillus niger*, *A. fumigatus*, *Acetobacter aceti*, *Penicillium chrysogenum*, and other *Penicillia*: Bernhauer, Schulof, U.S. pat. 1,849,053 (1932 to Pfizer); Williams, *Mfg. Chemist* 16, 239 (1945); Moyer *et al.*, *Ind. Eng. Chem.* 32, 1379 (1940); Prescott *et al.*, *ibid.* 45, 338 (1953); van Gelder, U.S. pat. 2,916,515 (1959 to Noury & van der Lande, Holland); Roehr, *Naturwiss.* 48, 478 (1961). Prepn by hydrolysis of  $\alpha$ -D-glucose with bromine +  $\text{H}_2\text{SO}_4$ : Foster, Vardheim, *J. Chem. Soc.* 1957, 989; by  $\gamma$ -irradiation of D-glucose: Phillips *et al.*, *ibid.* 1958, 3522; Grant, Ward, *ibid.* 1959, 2871. Prepn of solid: Isbell, U.S. pat. 1,985,255 (1934 to U.S. Secy of Commerce).



Crystals, mp 131°. Mild acid taste.  $[\alpha]_D^{20} -6.7'$  ( $c = 1$ ).  $K$  at  $25^\circ = 2.5 \times 10^{-4}$ . Freely sol in water, slightly sol in alcohol. Insol in ether and most other organic solvents. In aq solns the acid is partially transformed into an equilibrium mixt with gamma and delta gluconolactones. Because of the difficulties of preparing a solid cryst product, gluconic acid of commerce is a 50% aq soln, light amber color, faint odor of vinegar,  $d_4^{25} 1.24$ . May be stored in stainless steel drums.

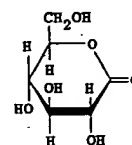
Ammonium salt,  $\text{NH}_4\text{C}_6\text{H}_{11}\text{O}_7$ . Needles, deliquescent in moist air and become yellow on exposure to light. Dec 154°. Neutral reaction. Soly in water: 31.6 g/100 ml at  $25^\circ$ . Slightly sol in alc. Practically insol in most other organic solvents. The salt dec on steaming with the formation of ammonia and gluconic acid.

Magnesium salt,  $\text{C}_{12}\text{H}_{24}\text{MgO}_{16}$ , *magnesium gluconate*, *Almora*, *Glucomag*, *Ultra-Mg*.

USE: See Gluconolactone. Ammonium salt used as latent acid catalyst in textile printing.

THERAP CAT: Magnesium salt as antispasmodic; in treatment of magnesium deficiencies.

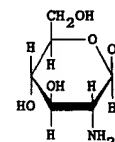
**4317. Gluconolactone.** D-Gluconic acid  $\delta$ -lactone; glucono delta lactone; delta gluconolactone.  $\text{C}_6\text{H}_{10}\text{O}_6$ ; mol wt 178.14. C 40.45%, H 5.66%, O 53.89%. Prepn by oxidation of glucose with bromine water: Isbell, Pigman, *J. Res. Nat. Bur. Stand.* 10, 337 (1933); by oxidation of glucose in *Acetobacter suboxydans*: King, Cheldelin, *Biochem. J.* 68, 31P (1958). Structure: J. Stanek *et al.*, *The Monosaccharides* (Academic Press, New York, 1963) p 271.



Crystals, dec 153°. Sweet taste (different from gluconic acid).  $[\alpha]_D^{20} +61.7'$  ( $c = 1$ ). Soly in water 59 g/100 ml; in alc about 1 g/100 g. Insol in ether. Hydrolyzed to gluconic acid by water. A freshly prepd 1% aq soln has a pH of 3.6 changing to pH 2.5 within 2 hrs.

USE: Component of many cleaning cmpds because of the sequestering ability of the gluconate radical which remains active in alk solns; in the dairy industry to prevent milkstone; in breweries to prevent beerstone; as latent acid catalyst for acid colloid resins, particularly in textile printing.

**4318. Glucosamine.** 2-Amino-2-deoxyglucose; chitosamine.  $\text{C}_6\text{H}_{13}\text{NO}_5$ ; mol wt 179.17. C 40.22%, H 7.31%, N 7.82%, O 44.65%. Found in chitin, in mucoproteins, and in mucopolysaccharides. Isola from chitin: Ledderhose, *Z. Physiol. Chem.* 2, 213 (1878); Hackman, *Aust. J. Biol. Sci.* 7, 168 (1954). Synthesis: Fischer, Leuchs, *Ber.* 35, 3787 (1902); 36, 24 (1903). Separation of  $\alpha$ - and  $\beta$ -forms: Westphal, Holzmann, *ibid.* 75B, 1274 (1942). Structure: Hawthorth *et al.*, *J. Chem. Soc.* 1939, 271; Cutler, Peat, *ibid.* 782; Cox, Jeffrey, *Nature* 143, 894 (1939). Review: Foster, Stacey, "The Chemistry of the 2-Amino Sugars" in C. S. Hudson *et al.*, *Advan. Carbohydr. Chem.* vol. 7 (Academic Press, New York, 1952) pp 247-288.



$\alpha$ -Form, crystals, mp 88°.  $[\alpha]_D^{20} +100^\circ \rightarrow +47.5^\circ$  after 30 min (water).

$\beta$ -Form, needles from methanol, dec 110°.  $[\alpha]_D^{20} +28^\circ \rightarrow +47.5^\circ$  after 30 min (water). Very sol in water, sol in about 38 parts boiling methanol; sparingly sol in cold methanol or ethanol. Practically insol in ether, chloroform.

N-Acetylglucosamine,  $\text{C}_8\text{H}_{15}\text{NO}_6$ , needles from methanol + ether, mp 205°.  $[\alpha]_D^{20} +64^\circ \rightarrow +40.9^\circ$  (in water).

THERAP CAT: Pharmaceutical aid.

**4319. Glucose.** D-Glucose; dextrose; blood sugar; grape sugar; corn sugar; Dextropur; Dextrosol; Glucolin.  $\text{C}_6\text{H}_{12}\text{O}_6$ ; mol wt 180.16. C 40.00%, H 6.72%, O 53.29%. A main source of energy for living organisms. Occurs naturally and in the free state in fruits and other parts of plants. Combined in glucosides, in di- and oligosaccharides, in the polysaccharides cellulose and starch, and in glycogen. Normal human blood contains 0.08-0.1%. Manuf on a large scale from starch: Dean, Gottfried, *Advan. Carbohydr. Chem.* 5, 127 (1950). Below  $50^\circ$ ,  $\alpha$ -D-glucose hydrate is the stable cryst form, above  $50^\circ$  the anhydri form is obtained and at still higher temps  $\beta$ -D-glucose is formed: W. Pigman, *The Carbohydrates* (Academic Press, New York, 1957) p 92. Structure: Kjaer, Lindberg, *Acta Chem. Scand.* 13, 1713 (1959). Conformation: E. Percival, *Structural Carbohydrate Chemistry* (J. Garnet Miller, London, 1962) pp 51-57. Comprehensive monograph: H. Bartelheimer *et al.*, *D-Glucose und*